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Evaluation of the systemic inflammatory response in patients with a spinal synovial cyst or lumbar disc herniation

Mustafa Öğden[1], Mustafa İlker Karagedik[1], İbrahim Umud Bulut[1], Mehmet Zengin[2], Ulaş Yüksel[1], Bülent Bakar[1]

[1]Department of Neurosurgery, Faculty of Medicine, Kırıkkale University, Kırıkkale, Turkey
[2]Department of Pathology, Faculty of Medicine, Kırıkkale University, Kırıkkale, Turkey

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Corresponding Author: Mustafa Öğden, mustafaogden38@gmail.com

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ABSTRACT

Aims: This study aimed to determine whether a systemic inflammatory response occurs in patients with spinal synovial cysts (SSC) and patients with lumbar disc herniation.

Methods: Patients who underwent surgery for SSC (SSC group) or lumbar disc herniation (LDH group) between 2016-2022 were included in the study. To compare the results of these patients, patients who applied to the outpatient clinic due to headaches but did not find any abnormal findings in the radiological examinations (Control group) were also included. Age, gender, duration of stay in the hospital, comorbidity, and histopathological evaluation results were recorded for all patients. The lumbar T2 weighted MR sagittal and axial images obtained on admission to the hospital were examined. The venous blood samples taken from the patients on first admission to the hospital were analyzed biochemically.

Results: There was no statistical difference among the SCC, LDH, and Control groups regarding age, gender, and blood biochemistry parameters. Furthermore, no statistical difference was found between SSC patients and patients with lumbar disc herniation in age, gender, cyst or herniated disc localization levels, comorbidity, and blood biochemistry analysis results. Correlation analysis for the findings of all patients revealed that no parameters were correlated with the study groups. ROC-Curve test and Logistic Regression tests showed that no parameter could be a predictive marker in differentiating SSC from disc herniation.

Conclusion: Study results demonstrated that neither SSC nor disc herniation caused a systemic inflammatory or allergic reaction in the patients. In addition, it was determined that no biochemical parameter could distinguish disc herniation from SSC.

Keywords: Spinal synovial cysts, lumbar disc herniation, systemic inflammation

INTRODUCTION

Spinal synovial cysts (SSC) include both synovial cysts and ganglion cysts arising from the facet joint or ligamentum flavum. These lesions are most commonly seen in the lumbar spine and at the L4-5 level (88-99%).[1] The etiology of SSC is unknown, but it can be seen together with degenerative disc disease, osteoarthritis, spondylolisthesis, spinal stenosis, and scoliosis accompanied by increased spinal instability, and the role of trauma is discussed.[2] Today, the first choice for the diagnosis of SSC is MR imaging. Especially on T2-weighted MR axial images, cysts are often located on the medial side of an abnormal facet joint and show osteoarthritic changes and irregular articular surfaces, as well as a hypertrophic or focally thickened ligamentum flavum.[3] The clinical and radiological differential diagnosis of SSC includes Tarlov perineural cyst, extradural arachnoid cyst, dermoid cyst, neuroma with cystic changes, herniated disc, and free fragments of intervertebral disc.[4-6]

SSC may remain silent in some patients or may resolve spontaneously over time. To explain the spontaneous resolution of the cyst, some authors hypothesize that the cyst ruptures spontaneously, while others argue that progressive degenerative changes in the facet joint cause successive fixation of previously hypermobile facets, thereby reducing intra-articular pressure and shrinking the cyst.[7] Sometimes the SSC may undergo degenerative changes, lose contact with the facet joint, and shrink due to nutrient deficiency.[8] It has been reported in the literature that NSAID therapy acts on both the synovium, subchondral bone, and cartilage of the spinal facet joints and therefore may affect several different physiological pathways involved in the pathogenesis of lumbar spine synovial cysts (such as inhibition of proteoglycan synthesis,

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induction of chondrocyte apoptosis and decreased production of cytokines and other mediators of inflammation). Therefore, it has been claimed that inhibition of inflammation in treating SSC may play an essential role in the pathogenesis of regression of lumbar spine synovial cysts.[9]

This study was conducted to determine whether a systemic inflammatory response occurs in patients with SSC. In addition, in this study, biochemical examination results of patients with SSC were compared with those of patients with lumbar disc herniation, and possible differences were tried to be revealed.

METHODS

Patients

The study was carried out with the permission of Kırıkkale University Medical Faculty Noninvasive Clinical Researches Ethics Committee (Date: 09.11.2022, Decision No: 2022/14-2022.11.06). A signed informed consent form was obtained from the patients.

Patients who underwent surgery for SSC or lumbar disc herniation between 2016-2022 were included in the study. To compare the results of these patients, patients who applied to the outpatient clinic due to headaches but did not find any abnormal findings in the radiological examinations were also included.

The working group was first divided into three groups as follows:

- Control group (n=14)
- CYST group (patients with a lumbar synovial cyst, n=13)
- LDH group (patients with single-level lumbar disc herniation, n=14)

Then, patients in the Control group who had an infection in the other facet joints, rheumatoid arthritis, other rheumatic diseases, bone metastases, or preoperative steroid injection were excluded from the study.

Materials

Age, gender, duration of stay in the hospital, and comorbidity (diabetes mellitus, hypertension, coronary artery disease, hypothyroidism, chronic obstructive pulmonary disease), were recorded for all patients. The lumbar T2 weighted MR sagittal and axial images obtained on admission to the hospital were examined in patients with SCC (**Figure 1**, **Figure 2**) and patients with lumbar disk herniation (**Figure 3**). Furthermore, Rosenstock classification type,[10] and NSURG classification[11] were evaluated in SCC patients. In addition, the histopathological analysis reports of all patients were recorded.

The venous blood samples taken from all individuals on first admission to the hospital were examined and the study results were obtained from these sample analyses. The blood hemoglobin level (reference range: 10-18 g/dL), leukocyte (reference range: 4400-11300 uL), neutrophil (reference range: 110-9600 uL), lymphocyte (reference range: 500-6000 uL), monocyte (reference range: 100-1400 uL), eosinophil (reference range: 0-1000 uL), basophil (reference range: 0-300 uL), and thrombocyte (reference range: 150,000-500,000 uL) count values were determined with an analysis device (Mindray BC-6800, Shenzhen, China). The erythrocyte sedimentation rate (ESR) value (reference interval <20 mm/hour) was measured by an automated system (ESR 40, Cystat Diagnostics). Furthermore, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio results (PLR), and lymphocyte-monocyte ratio (LMR) were evaluated.

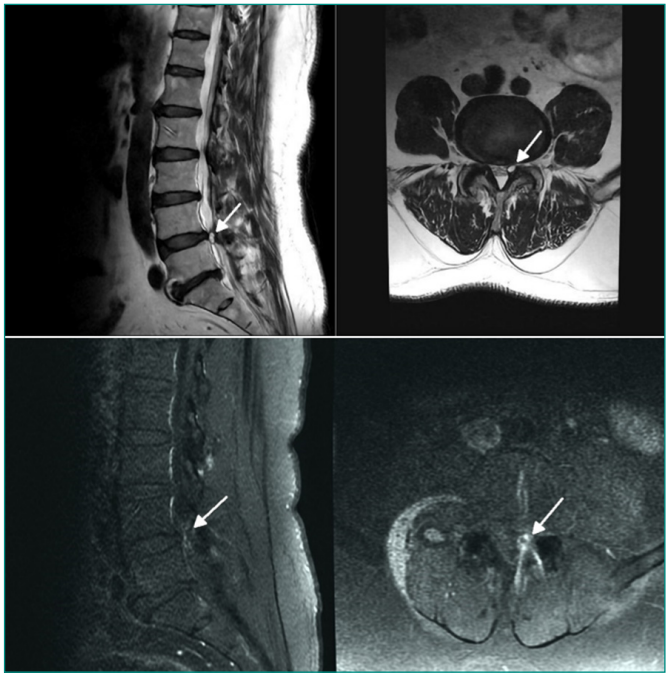

Figure 1. Microphotographs show T2-weighted MR axial images (1A) and T1-weighted MR axial images with gadolinium of a patient with a facet cyst.

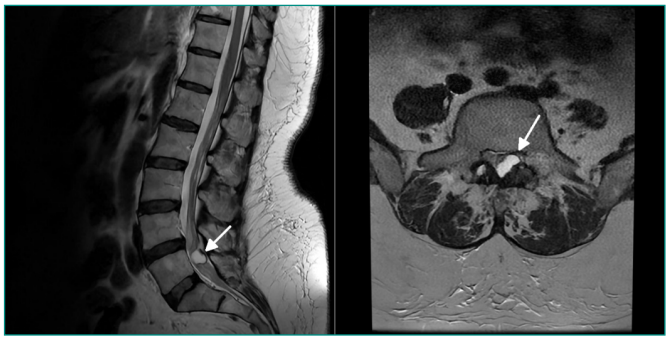

Figure 2. Microphotographs show T2-weighted MR axial images of a patient with a cyst of the ligamentum flavum.

Figure 3. Microphotographs show T2-weighted MR axial images of a patient with right-weighted disc herniation in the L3-4 level.

Serum glucose (reference range: 74-109 mg/dL), blood urea nitrogen (BUN) (reference range: 17-43 mg/dL), creatinine (reference range: 0.84-1.24 mg/dL), alanine aminotransferase (ALT) (reference range: 5-41 U/L), aspartate aminotransferase (AST) (reference range: 5-40 U/L), C-reactive protein (CRP) (reference range: 0.15-5 mg/dL), total protein (reference range: 6.40-8.30 g/dL), albumin (reference range: 3.50-5.20 g/dL), sodium (reference range: 136-146 mmol/L) and potassium (reference range: 3.5-5.1 mmol/L) levels were obtained using original kits (Roche) on an automatic device (Roche Diagnostic COBAS c501).

Surgery

While the patient was in the prone position under general anesthesia, the spinal level at which the surgical intervention would be performed was determined by fluoroscopy. A midline vertical skin incision was then made. After unilateral subperiosteal stripping of the paravertebral muscles at the relevant level, partial hemilaminectomy and flavectomy were performed. Flavum cyst, facet cyst (**Figure 4**, **Figure 5**), or herniated disc fragment (**Figure 6**) exerting pressure on nerve tissues were resected and placed in neutral formalin solution for future pathological examination. The surgical layers were closed by the anatomy and the operation was terminated.

Statistical Analysis

The categorical variables were analyzed using Pearson's chi-square test ($p<0.05$).

Parametric data were analyzed with One Way-Analysis of Variance (ANOVA) to evaluate the differences between groups ($p<0.05$). Non-parametric data were analyzed using the Kruskal-Wallis test ($p<0.05$). The Mann-Whitney U test was applied in the binary comparisons of the groups ($p<0.05$).

In addition, Spearman's rho Correlation test was used to determine the presence of correlation between parameters belonging to patients ($p<0.05$).

The ROC-Curve test was used to determine which study parameters predict the hematoma expansion and the mortality risk, and the sensitivity and specificity rates of the parameters were determined by obtaining "cut-off" values. In addition, the Logistic Regression test was used to determine the "best predictive parameter" ($p<0.05$).

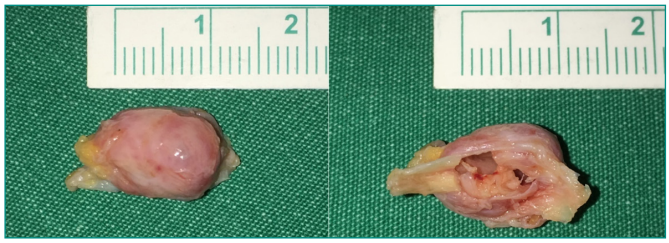

Figure 4. Macroscopic view of lumbar facet cyst.

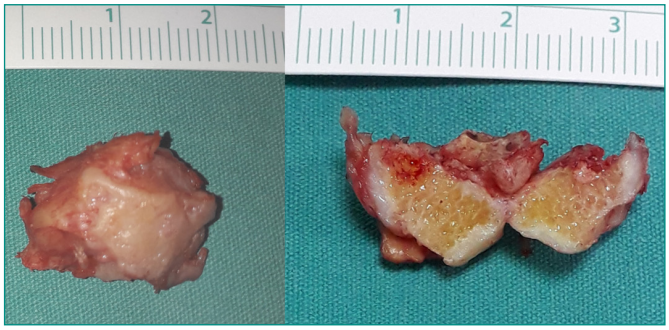

Figure 5. Macroscopic view of a lumbar facet cyst with dystrophic calcification.

Figure 6. Macroscopic view of herniated lumbar intervertebral disc.

RESULTS

A total of 13 SSC patients (**Table 1**), 14 lumbar disc herniation patients, and 14 individuals without any spinal disease were included in the study. In the SCC group, two patients had synovial cysts with dystrophic calcification (**Figure 5**), two had synovial cysts with hyalinization, one had a ganglion cyst, and one had a ligamentum flavum cyst. The remaining seven patients had simple SSC (**Figure 4**, **Figure 7**).

Table 1. Descriptive table of patients with spinal synovial cyst

Patient	Age	Sex	Hospitalization	Segment	Diabetes mellitus	Hypertension	Coronary artery disease	Hypothyroidism	Chronic lung disease	Rosenstock classification	NSURG classification			Histopathological diagnosis	Cyst diameters			
											Canal obstruction	Spondylolisthesis	Result		Length	Height	Width	Volume
1	74	F	4	L4-L5	-	+	-	-	-	2	0	0	1	Spinal ganglion cyst	10.5	5.61	4.9	144.3
2	74	F	2	L4-L5	+	-	-	-	-	2	0	0	1	Synovial cyst + dystrophic calcification	10.7	6.77	7.96	288.3
3	69	K	2	L3-L4	+	+	+	+	-	2	0	0	1	Degenerative synovial cyst + hyalinization	5.8	3.63	7.03	74.0
4	67	M	2	L4-L5	-	-	-	-	-	2	0	0	1	Synovial cyst	9.03	3.83	5.58	96.5
5	67	M	4	L5-S1	+	+	+	-	-	1	0	0	1	Synovial cyst	6.78	5.69	6.2	119.6
6	67	M	2	L2-L3	-	+	+	-	-	1	0	0	1	Ligamentum flavum cyst	13.8	6.86	9.42	445.9
7	67	M	12	L4-L5	-	-	-	-	-	1	0	0	1	Synovial cyst	25.2	15.1	13.3	2530.5
8	63	F	1	L4-L5	-	+	-	-	-	2	1	0	2	Degenerative synovial cyst + hyalinization	16.3	12.3	13.5	1353.3
9	53	F	2	L4-L5	+	+	-	-	+	3	0	0	1	Synovial cyst + dystrophic calcification	9.02	6.76	11.6	353.7
10	51	F	3	L4-L5	-	+	-	-	-	2	1	0	2	Synovial cyst	12.8	10.5	11.5	772.8
11	68	M	3	L4-L5	-	-	-	-	+	3	1	0	2	Synovial cyst	16.4	14.1	10.5	1214.0
12	60	F	3	L3-L4	+	+	-	-	-	2	0	1	4	Hemorrhagic synovial cyst	9.76	5.47	8.51	227.2
13	52	F	3	L3-L4	-	+	-	-	-	2	0	0	1	Synovial cyst	9.87	10	5.94	293.1

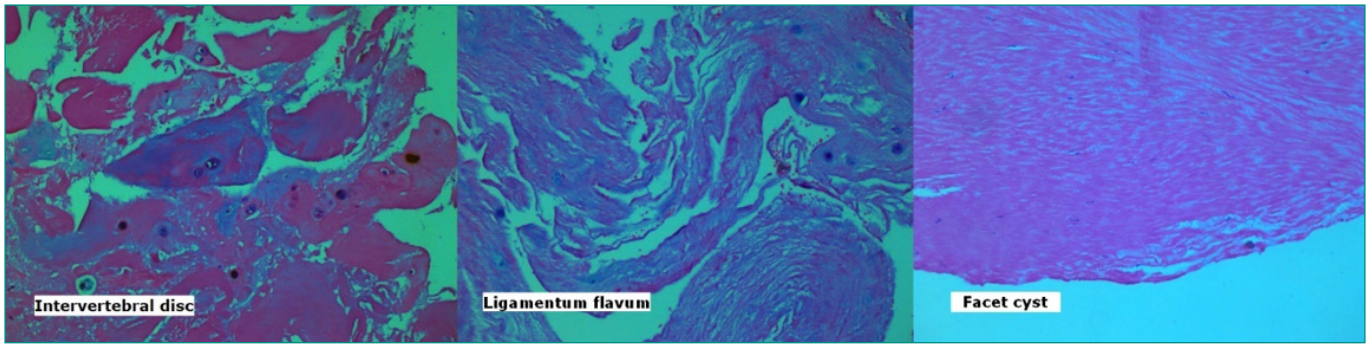

Figure 7. Histopathological examination images of a herniated intervertebral disc, a ligamentum flavum cyst, and a facet cyst.

It was found that the patients in the Control group were around 49 (34-69) years old, while the patients with SSC were around 67 (51-74) years old, whereas the patients in the LDH group were around 67 (36-89) years old. There was no statistical difference between the three groups in terms of age, gender, and blood biochemistry parameters (**Table 2**).

Table 2. Comparisons of the data of patients with spinal synovial cysts, patients with lumbar disc herniation, and the Control group patients.

Variable	Control	Cyst	LDH	F/ X2	p
	Mean ± SD Median (min-max)/ N (%)	Mean ± SD Median (min-max)/ N (%)	Mean ± SD Median (min-max)/ N (%)		
Age	49 (34-69)	67 (51-74)	67 (36-89)	-	-
Sex				0.659‡	0.719
Female	7 (29.2%)	8 (33.3%)	9 (37.5%)		
Male	7 (41.2%)	5 (29.4%)	5 (29.4%)		
Spinal level				1.639‡	0.651
L5-S1	-	1 (100.0%)	0 (0.0%)		
L4-5	-	8 (42.1%)	11 (57.9%)		
L3-4	-	3 (60.0%)	2 (40.0%)		
L2-3	-	1 (50.0%)	1 (50.0%)		
Hospitalization	-	3 (1-12)	2 (0-3)	-	-
Glucose	99.14±43.00	116.30±31.51	134.62±68.24	1.736†	0.190
BUN	29.14±7.35	36.63±7.64	37.18±12.56	3.072*	0.058
Creatinine	0.81±0.17	0.88±0.14	0.81±0.18	0.710*	0.498
ALT	24.50±10.65	24.23±16.47	26.61±14.70	0.118*	0.889
AST	25.50±12.24	19.66±7.15	22.12±8.06	1.301*	0.284
Protein	7.11±0.53	7.19±0.46	7.41±0.49	1.384*	0.263
Albumin	4.55±0.31	4.46±0.25	4.56±0.23	0.561*	0.575
CRP	3.06±3.98	3.30±3.19	4.77±5.68	0.607*	0.550
Sodium	141.14±2.14	140.82±2.66	140.04±2.41	0.776*	0.467
Potassium	4.75±0.41	4.79±0.29	4.70±0.39	0.229*	0.796
ESR	18.14±9.36	19.62±11.38	22.29±18.84	0.321*	0.728
Hemoglobin	14.51±1.36	13.79±2.05	14.21±1.35	0.668*	0.519
Leukocyte	6.40±1.71	5.18±1.92	5.90±3.17	0.901*	0.415
Platelet^10³	305±123334.26	279±76771.60	257±70651.91	0.939*	0.400
Neutrophile	2.15±0.85	2.13±0.79	2.69±1.49	1.167*	0.322
Basophil	32.14±18.88	30.00±15.28	36.43±19.85	0.441*	0.646
Eosinophil	162.14±95.69	214.62±219.11	183.57±113.38	0.412*	0.665
Monocyte	422.86±132.28	457.69±104.34	462.14±121.10	0.445*	0.644
NLR	2.15±0.85	2.13±0.79	2.69±1.49	1.167*	0.322
PLR	120.90±35.71	131.11±49.67	112.86±36.20	0.676*	0.514
LMR	6.40±1.71	5.18±1.92	5.90±3.17	0.901*	0.415

(*) F value, One Way-Analysis of Variance test; (†) X2 value, Kruskal Wallis test; (‡) X2 value, Pearson' s Chi-square test; p <0.05

At the end of the statistical analyzes performed by excluding the Control group, no statistical difference was found between SSC patients and patients with lumbar disc herniation in terms of age, gender, cyst or herniated disc localization levels, and comorbidity. In addition, no difference was found between these two patient groups in terms of blood biochemistry analysis results. However, a statistical difference was found between the two groups in terms of length of stay in the hospital (X2=-2.409, p=0.016) (**Table 3**).

Table 3. Comparisons of the data of patients with spinal synovial cysts and patients with lumbar disc herniation.

Variable	Cyst	LDH	F/ X2	p
	Mean ± SD Median (min-max)/ N (%)	Mean ± SD Median (min-max)/ N (%)		
Age	67 (51-74)	67 (36-89)	-0.271†	0.786
Sex				
Female	8 (47.1%)	9 (52.9%)	0.022‡	0.883
Male	5 (50.0%)	5 (50.0%)		
Level				
L5-S1	1 (100.0%)	0 (0.0%)	1.639‡	0.651
L4-5	8 (42.1%)	11 (57.9%)		
L3-4	3 (60.0%)	2 (40.0%)		
L2-3	1 (50.0%)	1 (50.0%)		
Hospitalization	3 (1-12)	2 (0-3)	-2.409†	0.016
Glucose	116.30±31.51	134.62±68.24	-0.884*	0.385
BUN	36.63±7.64	37.18±12.56	-0.137*	0.892
Creatinine	0.88±0.14	0.81±0.18	1.119*	0.274
ALT	24.23±16.47	26.61±14.70	-0.398*	0.694
AST	19.66±7.15	22.12±8.06	-0.838*	0.410
Protein	7.19±0.46	7.41±0.49	-1.220*	0.234
Albumin	4.46±0.25	4.56±0.23	-1.071*	0.294
CRP	3.30±3.19	4.77±5.68	-0.823*	0.418
Sodium	140.82±2.66	140.04±2.41	0.802*	0.430
Potassium	4.79±0.29	4.70±0.39	0.708*	0.485
ESR	19.62±11.38	22.29±18.84	-0.441*	0.663
Hemoglobin	13.79±2.05	14.21±1.35	-0.625*	0.538
Leukocyte	5.18±1.92	5.90±3.17	-0.708*	0.485
Platelet^10³	279±76771.60	257±70651.91	0.760*	0.454
Neutrophile	2.13±0.79	2.69±1.49	-1.212*	0.237
Basophil	30.00±15.28	36.43±19.85	-0.938*	0.357
Eosinophil	214.62±219.11	183.57±113.38	0.467*	0.644
Monocyte	457.69±104.34	462.14±121.10	-0.102*	0.920
NLR	2.13±0.79	2.69±1.49	-1.212*	0.237
PLR	131.11±49.67	112.86±36.20	1.097*	0.283
LMR	5.18±1.92	5.90±3.17	-0.708*	0.485

(*) t value, Independent Samples t test; (†) Z value, Mann Whitney U test; (‡) X2 value, Pearson' s Chi-square test; p <0.05

At the end of the correlation analysis for the findings of all patients, it was determined that no parameters were correlated with the study groups. As a result of the ROC-Curve test and Logistic Regression tests, it was concluded that no parameter could be a predictive marker in differentiating facet cysts from disc herniation.

DISCUSSION

SSC is symptomatic in many patients (90%) and may cause low back and leg pain.[12] It has been suggested that conservative treatment options such as physiotherapy, anti-inflammatory painkillers, and local steroid applications should be used primarily in treating symptomatic SSC, and surgical intervention should be applied when these treatments are insufficient. Percutaneous procedures

have been shown to have a statistically significantly lower symptom resolution rate than decompressive procedures.[13] There are three main treatment methods in the surgical treatment of SCC: percutaneous cyst aspiration, decompression surgery (hemilaminectomy, partial laminectomy, total laminectomy, etc.), and decompression surgery with fusion. While decompression surgery is sufficient in most patients, decompression with fusion is recommended for patients with spinal instability.[12] In our study, patients were treated with anti-inflammatory painkillers and physiotherapy, but local steroid therapy and/ or percutaneous cyst aspiration were not applied. Since none of the patients benefited from conservative treatments, hemilaminectomy, flavectomy, and cyst excision were performed by the microsurgical method, but fusion was not attempted. It was determined that the symptoms of all SSC patients improved after surgery.

It has been argued that ganglion cysts develop from mucinous degeneration of connective tissue in the mobile spine and have no direct connection with the facet joint. Besides, it has been claimed that synovial cysts are caused by laxity of the synovium of the facet joints, and therefore, they are highly correlated with segmental instability.[6] However, in our study, grade 1 spondylolisthesis was detected in only one patient. Since instability was not detected in this patient's preoperative standing lateral flexion and extension radiographs, decompression was performed, but fusion was not performed. Therefore, it was thought that SSC in these patients could not be related to instability.

On the other hand, it has been shown that the incidence of SSC is higher in patients with spondyloarthropathy, and it has been claimed that facet joint inflammation has an important role in the formation and development of SSC.[14] In addition, some studies have shown that angiogenic factors are released during the formation of synovial cysts, suggesting that these new vessels may increase the proliferation of synovial structures and that these factors may be associated with chronic inflammatory processes accompanying the progression of synovial cysts.[15] Many of these cysts have been shown to contain peculiar fine granular basophilic calcification, usually associated with a foreign body giant cell reaction and surrounding vascular and fibroblastic/ myofibroblastic proliferation.[16,17] For these reasons, it has been claimed that inhibition of inflammation in the treatment of SSC may play an important role in the pathogenesis of regression of lumbar spine synovial cysts.[9]

However, in a study, it was reported that after local steroid injections were applied to patients with SSC-related radicular pain, an excellent or good clinical result was obtained in 36% of patients in long-term follow-up, but additional steroid injections were made in one-third of these patients. It has been reported that in patients with moderate or poor results and patients with recurrent pain, repeated steroid injections were ineffective and eventually required surgery in these patients.[18] In another study, it was reported that in SSC patients, percutaneous cyst rupture or local intra-articular steroid injections were not superior to each other, both methods had an excellent short-term pain relief effect, but the effect decreased over time. Therefore, it has been said that percutaneous cyst rupture or local steroid injections can reduce the need for surgery in a significant number of patients and therefore may be recommended as first-line therapy, especially for those at high surgical risk.[19]

In our study, two SSC patients had dystrophic calcification and two had hyalinization. The remaining seven patients had simple SSC, one had a ganglion cyst, and one had a ligamentum flavum cyst. On the other hand, in the histopathological examinations, no chronic inflammation or foreign body giant cell reaction was detected in the specimens of the other patients, except for one patient. In addition, when the results of the biochemical analysis were examined, it was observed that there was no increase in inflammatory cytokine (CRP) or increase in inflammatory cells. With these findings, it was thought that these cysts did not induce systemic inflammatory reactions. In addition, it was observed that both groups' biochemical results were similar to those of the Control group individuals. In particular, CRP, leukocyte, neutrophil, lymphocyte, monocyte, eosinophil, and basophil values were observed to be similar in all three groups. In addition, ESR, NLR, PLR, and LMR values were found to be similar. These findings showed that neither SSC nor herniated discs caused a systemic inflammatory or allergic response. With these findings, it was considered that the cause of axial and or radicular pain in these patients was not due to systemic inflammatory reactions. Therefore, it was thought that the NSAIDs used in these patients were effective in suppressing or regressing the local inflammatory response and edema secondary to the lack of nutrition and hypoxia in these neural tissues during the pressure exerted by the SSC or disc fragment on the neural tissues, and thus they could reduce the pain and symptoms in the patients. However, this study could not support this hypothesis, since local inflammatory cytokines at the distance of SSC and herniated disc could not be measured in these patients.

On the other hand, it was determined that none of the biochemical parameters used in the study could distinguish disc herniation from SSC. This was thought to be due to the similar biochemical results in both groups.

CONCLUSION

As a result, it was determined that neither SSC nor disc herniation caused a systemic inflammatory or allergic reaction in the patients. In addition, it was determined that no biochemical parameter could distinguish disc herniation from SSC.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Kırıkkale University Medical Faculty Noninvasive Clinical Researches Ethics Committee (Date: 09.11.2022, Decision No: 2022/14-2022.11.06).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Mustafa Öğden

I graduated from Karadeniz Technical University Medical Faculty in 1999. Between 2000 and 2006, I completed my neurosurgery specialization at Erciyes University. After working in various public and private hospitals for 9 years, I started Kırıkkale University as an Assistant Professor in 2015. I became an associate professor in 2020, I am still actively working at Kırıkkale University Faculty of Medicine.